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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,743	12/20/2005	Efthimios Ippikoglou	02901/0203760-US0	8279
7278	7590	04/30/2007		
DARBY & DARBY P.C. P. O. BOX 5257 NEW YORK, NY 10150-5257			EXAMINER BASI, NIRMAL SINGH	
			ART UNIT	PAPER NUMBER
			1646	
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			04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/561,743	Applicant(s) IPPIKOGLU, EFTHIMIOS	
	Examiner Nirmal S. Basi	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-37 is/are pending in the application.
- 4a) Of the above claim(s) 30-32, 34-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Amendments filed 2/15/07 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claim 33 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Lustbader (US Patent number 7,081,446) in view of Florkiewicz (Patent No. 5891855) and further in view of Boime et al. (Patent No. 6238890) for reasons of record as set forth in the previous office action.

Applicant argues:

Obviousness requires that each and every claim limitation be disclosed or suggested by the prior art. None of the cited references alone or in combination disclose or suggest the instant invention because they do not disclose or suggest chimeric protein comprising an alpha FSH subunit fused in frame with the beta FSH subunit and produced as a single polypeptide chain without a linker or enhancer moiety. In contrast, Lustbader's teachings are solely directed to chimeric FSH polypeptides containing linker segments for improved stability. Nowhere does Lustbader teach or suggest making the presently claimed fusion polypeptide where the alpha FSH subunit is fused in frame with the beta FSH subunit and produced as a single polypeptide chain without a linker or enhancer moiety. All of the chimeric polypeptides described by Lustbader contain linker or enhancer segments. Furthermore, Lustbader provides no suggestion that creating an alpha +beta FSH fusion protein without linker sequences, as reflected in the presently claimed fusion polypeptide of SEQ ID NO:27, would be successful. Thus, Lustbader cannot provide a motivation to combine the alpha and beta FSH subunits without linker sequences. Furthermore, Lustbader provides no data with regard to the activity (reflecting expectation of success) of an alpha +beta FSH fusion protein without linker sequences.

Applicant's arguments have been fully considered but they are not found persuasive.

Firstly, to clarify the record it is noted that claim 33 is directed to a polypeptide

comprising the amino acid sequence set forth in SEQ ID NO:27. The comprising claim language is open ended and reads on polypeptides that have linker sequences in addition to the sequence set forth in SEQ ID NO:27.

Claim 33 is drawn to a polypeptide (chimeric FSH molecule) comprising the amino acid sequence set forth in SEQ ID NO:27 (i.e. an alpha-FSH subunit and beta-FSH subunit construct).

Lustbader teaches a synthetic chimeric FSH construct comprising an alpha-FSH subunit and a beta-FSH subunit.

Lustbader teaches the following embodiments:

- A. A synthetic FSH comprising a beta-FSH subunit, an alpha-FSH subunit and a half-life-increasing moiety, wherein the beta-FSH subunit, an alpha-FSH subunit and half-life-increasing moiety are covalently bound.
- B. A synthetic FSH comprising a beta FSH subunit, an alpha-FSH subunit and a polypeptide segment comprising the amino acid sequence ser-gly-ser-asn-ala-thr-gly-ser-gly-ser-asn-ala-thr-ser-gly-ser, (SEQ ID NO:9), wherein the beta-FSH subunit, an alpha-FSH subunit and polypeptide segment are covalently bound.
- C. The beta-FSH subunit, an alpha-FSH subunit are bound to each other via the half-life-increasing moiety, and in a preferred embodiment, the beta-FSH subunit, the alpha-FSH subunit and the polypeptide segment exist within a single polypeptide chain. In one embodiment, the beta-FSH subunit is bound at its C-terminal end to the N-terminal end of the polypeptide segment, or conversely, the beta-FSH subunit is bound at its N-terminal end to the C-terminal end of the polypeptide segment.
- D. A synthetic FSH wherein the beta-FSH subunit is bound at its C-terminal end to the N-terminal end of the polypeptide segment, and the polypeptide segment is bound at its C-terminal end to the N-terminal end of the alpha-FSH subunit.
- E. A synthetic FSH wherein the alpha-FSH subunit is bound at its C-terminal end to the N-terminal end of the polypeptide segment, and the polypeptide segment is bound at its C-terminal end to the N-terminal end of the beta-FSH subunit. In a further embodiment, the synthetic FSH comprises the N-terminal signal sequence of either the beta-FSH or alpha-FSH subunit. In an embodiment of any of the instant synthetic FSHs,

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the alpha-FSH subunit (if applicable) and beta-FSH subunit are from an animal selected from the group consisting of a primate, a horse, a sheep, a bird, a bovine, a pig, a dog, a cat, and a rodent. In the preferred embodiment, the alpha-FSH and/or beta-FSH subunit is a human subunit. In a further preferred embodiment, the alpha-FSH subunit (if applicable) and the beta-FSH subunit exist within a single polypeptide chain along with the half-life-increasing moiety.

G. A method for producing a synthetic FSH, which comprises co-expressing (i) a nucleic acid which encodes an alpha-FSH subunit, and (ii) a nucleic acid which encodes a polypeptide comprising a beta-FSH subunit and a polypeptide segment comprising the amino acid sequence ser-gly-ser-asn-ala-thr-gly-ser-gly-ser-asn-ala-thr-ser-gly-ser under conditions permitting such co-expression; and recovering the synthetic FSH so produced.

Lustbader does not disclose the synthetic chimeric polypeptide consisting of the alpha-FSH and beta-FSH disclosed in SEQ ID NO:27.

Florkiewicz (Patent No. 5891855) teaches the alpha-FSH subunit (SEQ ID NO:5) which is identical to amino acids 1-116 of SEQ ID NO:27 of instant application.

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Query Match          50.5%;  Score 643;  DB 1;  Length 116;
Best Local Similarity 100.0%;  Pred. No. 8.7e-53;
Matches 116;  Conservative 0;  Mismatches 0;  Indels 0;  Gaps
0;

Qy          1 MDYYRKYAAIFLVTLVFLHVLHSAPDVQDCPECTLQENPFFSQPGAPILQCMGCCFSRA 60
            |||
Db          1 MDYYRKYAAIFLVTLVFLHVLHSAPDVQDCPECTLQENPFFSQPGAPILQCMGCCFSRA 60

Qy          61 YPTPLRSKKTMLVQKNVTSESTCCVAKSYNRVTVMGGFKVENHTACHCSTCYHKS 116
            |||
Db          61 YPTPLRSKKTMLVQKNVTSESTCCVAKSYNRVTVMGGFKVENHTACHCSTCYHKS 116
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Boime (Patent No. 6238890) teaches beta-FSH subunit (SEQ ID NO:12) which is identical to amino acids 117-227 of SEQ ID NO:27 of instant application.

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Query Match          49.5%;  Score 630;  DB 2;  Length 229;
Best Local Similarity 100.0%;  Pred. No. 3.2e-51;
Matches 111;  Conservative 0;  Mismatches 0;  Indels 0;  Gaps
0;
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Qy      117 NSCELTNITIAIEKEECRFCISINTTWCAGYCYTRDLVYKDPARPKIQKTCTFKELVYET 176
          |||
Db      19 NSCELTNITIAIEKEECRFCISINTTWCAGYCYTRDLVYKDPARPKIQKTCTFKELVYET 78

Qy      177 VRVPGCAHHADSLYTPVATQCHCGKCDSDSTDCTVRGLGPSYCSFGEMKE 227
          |||
Db      79 VRVPGCAHHADSLYTPVATQCHCGKCDSDSTDCTVRGLGPSYCSFGEMKE 129

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It would have been obvious for one of ordinary skill in the art to use the method disclosed by Lustbader to construct a synthetic FSH chimeric polypeptide comprising an alpha-FSH subunit and beta-FSH subunits taught by Florkiewicz and Boime, with or without the half-life-increasing moiety as disclosed by Lustbader, to construct molecules with different half lives. One of ordinary skill in the art would have been motivated to construct such a polypeptide based on the teaching of Lustbader, which show that, the half life of FSH chimeric polypeptide can be increased or decreased depending on which life-increasing moiety is used. One of ordinary skill in the art would have had a reasonable expectation of success in constructing a chimeric polypeptide comprising an alpha-FSH subunit and a beta-FSH subunit because Lustbader routinely constructed similar types of molecules. Therefore, the claimed invention was obvious at the time of the invention.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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